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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,026	11/21/2003	Madaline Chirica	DX01074B1K	3154

28008 7590 08/09/2007

DNAX RESEARCH INC.
LEGAL DEPARTMENT
901 CALIFORNIA AVENUE
PALO ALTO, CA 94304

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	**PAPER NUMBER**
1647	
MAIL DATE	**DELIVERY MODE**
08/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/720,026	CHIRICA ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5,6,8 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is in response to Applicant's remarks and amendments filed 5/29/2007. Applicant has cancelled claims 7 and 10-17 as drawn to non-elected subject matter. Claims 2 and 4 remain withdrawn as they are drawn to unelected species. Claims 1, 5 and 8 are amended. Therefore, claims 1, 3, 5, 6, 8 and 9 are examined.

2. Any objection or rejection of record, which is not expressly repeated in this action, has been overcome by Applicant's response and withdrawn.

Priority

3. Based on the support found in U. S. Provisional Application No. 60/203, 426 Applicant is entitled to the priority date of 5/10/2000.

Claim Rejections - 35 USC § 112 1st paragraph, maintained

4a. The rejection of claims 1, 3, 5, 6, 8 and 9 under 35 U.S.C. 112, first paragraph is maintained, because the specification while enabling for a method of treating a human subject experiencing a physiological disorder comprising administering an effective amount antagonist antibody, does not provide enablement for all antagonists including nucleic acid. The reasons for rejection were set forth in the Office Action dated 2/27/07 (pages 8-10). Specifically, claims 1, 8 and 9 recite antagonist that are nucleic acids. However, the Office did not discuss the nucleic acid as antagonist previously.

Problems related to therapeutic use of nucleic acids (antisense and RNAi) were well known in the art at the time of invention (see for example Opalinska et al. (Nature Reviews Drug Discovery, 2002, vol. 1, p. 503-514)). Such problems include the inability

to specifically deliver an effective concentration of a nucleic acid to a target cell or tissue, such that a target gene is inhibited to a degree necessary to result in a therapeutic effect.

Opalinska et al. state on page 511

> "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA"

and in column 2 of the same page,

> "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

Given this unpredictability, the skilled artisan would require specific guidance to practice the claimed methods *in vivo* in humans, with a resultant inhibition of gene expression, as claimed. The specification provides ***no examples*** for the administration of nucleic acid for the treatment. In the absence specific teachings it is unclear how the nucleic acid antagonist will function to regulate DCRS5 (SEQ ID NO: 2). In addition, the post filing art provided with response of 5/29/2007 does not predict or teach *in vivo* inhibition (regulation) using nucleic acid as an antagonist. The genetic knock out studies reported in Duerr et al. do not provide guidance for the nucleic acids contracts that may be used as antagonists or for the method of administration. Duerr et al. also eludes a murine colitis model that is worsened in the absence of IL-23. Further, there are no methods of delivery of the nucleic acid to humans in the specification. Based on the teachings of Opalinska et al. reference, the uptake and biological activity observed

following nucleic acid antagonist administration would not be predictable. Given these teachings, the skilled artisan would not know *a priori* whether introduction of nucleic acids *in vivo* as broadly claimed in the instant invention, would result in the nucleic acid reaching the proper cell or tissue in a sufficient concentration and remaining for a sufficient time to provide successful inhibition or down regulation of expression of a target gene. In fact, the state of the art is such that successful delivery of nucleic acid sequences *in vivo*, such that the nucleic acids provides the requisite biological effect to the target cells/tissues/organs, must be determined empirically.

The specification does not provide the guidance required to overcome the art-recognized unpredictability of using nucleic acids in therapeutic applications in any organism and specifically in humans. The teachings of the prior art do not provide that guidance, such that the skilled artisan would be able to practice the claimed therapeutic methods.

Thus, while the specification is enabling for the examples set forth in the specification, the specification is not enabling for ***the broad claims of antagonizing the expression of DCRS 5 in humans*** as the art of inhibiting gene expression by introducing antisense nucleic acid or RNA interference (RNAi) into an organism is neither routine nor predictable. The amount of experimentation required is such that one of skill in the art could not practice the invention commensurate in scope with the claims without undue, trial and error experimentation and therefore, claims 1, 3, 5, 6, 8 and 9 are not enabled. Thus, the rejection of record is maintained.

4b. The rejection of claims 1, 3, 5, 6, 8 and 9 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Although, Applicant has provided written description support for antagonists that are antibodies there is no *written description* support for nucleic acid as antagonists. Specifically, claims 1, 8 and 9 recite antagonist that are nucleic acids. However, the Office did not discuss the nucleic acid as antagonist previously in the Office Action of 2/27/07.

Specifically, Applicant does not provide written description support for the various antisense nucleic acids and RNA interference nucleic acids contemplated in the instant invention. The claims as written, however, encompass antagonists of DCRS5 which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1, 3, 5, 6, 8 and 9. The specification does not provide written description to support the genus encompassed by the instant claims. With the exception of antibody that binds DCRS5, the skilled artisan cannot envision all the detailed chemical structure of the claimed antagonists regardless of the complexity or simplicity of the method of isolation. Therefore, only the antibodies that act as antagonists but not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. Therefore, the rejection of record is maintained.

Claim Rejections - 35 USC § 112 2nd paragraph, (new)

5a. Claims 1 and 5 are rejected as vague and indefinite in the recitation of "a binding composition derived from the antigen binding site of an antibody". It is unclear which compositions derived from the antigen binding site of antibody will function as antagonists. For example, will short polypeptides that are derived from antigen binding site of DCRS5 function as antagonist? One of skill in the art would not be able to determine which compositions act as antagonist off DCRS5. Claims 3, 6, 8 and 9 are rejected insofar as they are dependent on rejected claims 1 and 5.

5b. Claim 1 is rejected as vague and indefinite in the recitation of "an antagonist of DCRS5 (SEQ ID NO: 2)". It is unclear if SEQ ID NO: 2 is representative of DCRS5 or the antagonist contemplated by the Applicant is for SEQ ID NO: 2. It is suggested that Applicant rewrite the claim to indicate that the antagonist contemplated is for DCRS5 of SEQ ID NO: 2. Claims 3, 5, 6, 8 and 9 are rejected insofar as they are dependent on rejected claim 1.

6. No claims are allowable.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph. D can be reached on 571-272-0835. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
Art Unit 1647
August 3rd, 2007.

Jegatheesan Seharaj
Patent Examiner